



Ox-CERPC
Oxford Centre for Education and Research in Palliative Care

Nausea and Vomiting

New drug approaches in practice

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Nausea and Vomiting

- **Nausea** - unpleasant sensation of the need to vomit, often accompanied by autonomic symptoms (pallor, cold sweat, salivation, tachycardia).
- **Vomiting** - forceful ejection of stomach contents through the mouth.



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Prevalence

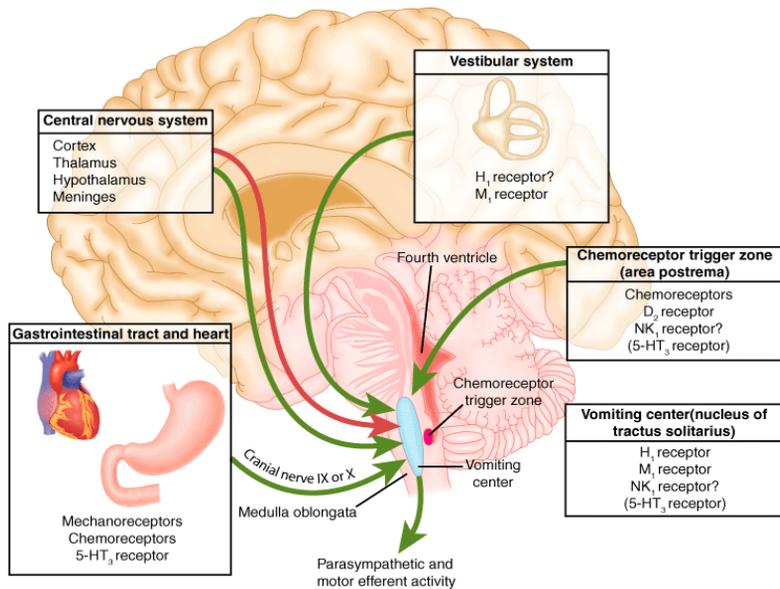
- Cancer patients
 - Chemotherapy and radiotherapy.
 - Acute, delayed and anticipatory.
 - 30-60% of patients at the end of life report nausea.
 - Frequently reported symptom, longitudinal studies suggest *intensity* is low (over six month period).
- Other palliative patients
 - Nausea – reported in end stage of all diseases
 - Most frequently in patients with CKD and HF (30-40%).
- 70% report nausea in the final week of life.

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Pathophysiology

- Chemotherapy Trigger Zone (CTZ)
 - Floor of 4th ventricle.
 - Lacks blood brain barrier.
 - Detects emetic agents in the bloods (toxins, drugs, metabolites).
 - Activates dopamine 2 receptors.
- The Vomiting Centre (VC)
 - Anatomically indistinct area of medulla oblongata.
 - Collates input from CTZ, vestibular system, higher cortical centres and thoracoabdominal organs
 - Vomiting reflex is co-ordinated by the VC in the brainstem, not requiring input from the cortex.

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Source: Katzung BG, Masters SB, Trevor AJ: *Basic & Clinical Pharmacology*, 11th Edition: <http://www.accessmedicine.com>
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Anti-emetic	Dopamine D ₂ antagonist	Histamine H ₁ antagonist	Acetylcholine antagonist	5-HT ₂ antagonist
Metoclopramide*	++	–	–	–
Domperidone†	++	–	–	–
Cyclizine	–	++	++	–
Hyoscine	–	–	+++	–
Haloperidol	+++	–	–	–
Levomepromazine	++	+++	++	+++

– none or insignificant;

+ slight; ++ moderate; +++ marked.

* Metoclopramide in higher doses ≥ 100 mg, demonstrates 5-HT₃-receptor antagonism.

† Domperidone does not cross the blood brain barrier so the risk of extrapyramidal adverse effects (such as tremors, slurred speech, and dystonia) is negligible.

Information from: [\[Twycross, 2014\]](#)

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Identify a cause.

- Consider nature of the underlying condition(s)
- Bowel habit – constipation.
- Hypercalcaemia (constipation, confusion, dehydration).
- Raised intracranial pressure (headache, worsening morning symptoms).
- Anxiety.
- Medications including NSAIDs.

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	Cause	Mechanism
Chemical	Drugs (opioids) Metabolic (hypercalcaemia) Toxins (food poisoning/ischaemic bowel)	Stimulate the CTZ Cytotoxic drugs cause vagal receptor stimulation.
Gastrointestinal stretch or irritation	Drugs e.g NSAIDs Constipation Intestinal obstruction Liver metastases	Mechanoreceptors in the gut stimulate the vagus acting on the vomiting centre.
Increased Intracranial pressure	Tumour or bleed Oedema Meningeal/skull mets	Cerebral histamine receptors.

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	Cause	Mechanism
Gastric stasis	Drugs (opioids, anticholinergics) Ascites, hepatomegaly Peptic ulcer Gastritis Autonomic failure	Gastric receptors stimulate the vagus nerve which acts on the vomiting centre.
Movement related	Opioids Gut distortion Gastroparesis	Opioids increase sensitivity of vestibular nerves. Gut mechanoreceptors stimulate the vagus nerve.
Anxiety related	Generalised anxiety Anticipatory vomiting	Cerebral cortex is stimulated – acts on the vomiting centre.

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Non-pharmacological approaches

- Minimise sights and sounds of food preparation, noxious smells.
- Small meals – snacking maybe preferable.
- Carbohydrate-based meals.
- Access to sick bowl, water and tissues.
- Complementary therapies:
 - Acupuncture/pressure bands – unknown benefit but overall high safety.
 - Ginger – may help some.

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Pharmacological Approaches

- Drug induced and metabolic causes:
 - correct the correctable.
 - Haloperidol 1.5mg Nocte or bd
- Intracranial disease or movement related:
 - Cyclize 25mg-50mg tds
 - consider dexamethasone.
- Bowel obstruction:
 - Sub acute (peristaltic failure) – Metoclopramide 10mg tds.
 - Bowel obstruction
 - Cyclizine; Cyclizine and haloperidol; levomepromazine.
 - Hyoscine also likely to be of benefit.

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Pharmacological approaches

- Gastric stasis:
 - Metoclopramide 10mg – 20mg tds.
- Anxiety:
 - Benzodiazepine, levomepromazine.
- If not working:
 - Ensure maximal dose of medication.
 - Likely to require more than one anti-emetic.
 - Refer to Palliative Medicine if not controlled.

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Olanzapine

- Second generation atypical antipsychotic.
- Broad spectrum neurotransmitter blockade (5HT_{2,3} and 6, D₁₋₄, Alpha adrenergic, acetylcholine and H₁ histamine receptors).
- Oral administration (2.5mg to 10mg)
- Cautions – Extra Pyramidal side effects, QTc prolongation and rarely neutropenia.
- Increase in fatigue – may also have an impact on anorexia and possibly anxiety and depression.
- With thanks to Dr Anna Sutherland

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Aprepitant

- Neurokinin-1 receptor antagonist - Works by blocking substance P attaching to NK1 receptors.
- Most frequently used in preventing Chemotherapy induced nausea and vomiting, alongside steroids and ondansetron.
- Case reports of use in palliative care, refractory nausea and vomiting.
- Role in managing nausea in Cystic Fibrosis patients.
- Well tolerated drug, fatigue very occasionally hiccups.

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Cannabinoids

- Nabilone and Sativex
- Used in Chemotherapy induced nausea and vomiting in refractory cases based on a Cochrane review.
- Sometimes used in the TYA population.
- No real role in managing most palliative patients.



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Alcohol wipes for nausea?

- 80 patients in Emergency Department.
- Randomised to inhaled isopropyl alcohol or normal saline.
- Significant improvement in nausea, but not prolonged.



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Summary

- Nausea and vomiting is common in palliative patients.
- Identify a cause if possible, reverse the reversible.
- Select an anti-emetic based on the most likely cause, many multifactorial.
- New agents Olanzapine and Aprepitant emerging – unclear where they sit currently.
- Please involve Palliative Care.

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Questions



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